General

Guideline Title

Blood transfusion: indications, administration and adverse reactions.

Bibliographic Source(s)

Finnish Medical Society Duodecim. Blood transfusion: indications, administration and adverse reactions. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2011 Aug 15 [Various].

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Blood transfusion: indications and administration. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2008 Jan 10 [Various].

Recommendations

Major Recommendations

Essentials

- Donated blood is not transfused to the recipient until it has been processed into its separate blood components.
- Red cells are transfused in anaemia to provide adequate oxygen delivery.
- Plasma (Octaplas®) is transfused in haemorrhage to provide coagulation factors when the haemorrhage is not caused by the deficiency of a single coagulation factor.
- Platelets (i.e., thrombocytes) are indicated for the management of bleeding or in thrombocytopenia to promote haemostasis when the platelet number or function is insufficient.
- In primary care, the use of blood products is limited to the treatment of symptomatic chronic anaemia when no alternative treatment is available.
- Platelet transfusions may also occasionally be administered outside hospital, for example to patients with haematological diseases.

Red Cell Transfusion

Chronic or Slowly Developing Anaemia

- It is not possible to give a single haemoglobin (Hb) value as a trigger for red cell transfusion since the requirement for a transfusion is based on the patient's underlying condition and symptoms.
    - Red cell transfusions are not routinely recommended for the correction of anaemia in patients with malignant or serious chronic

diseases, unless the correction of Hb concentration is expected to significantly improve the patient's condition and independence.

- Most patients will suffer uncomfortable symptoms of anaemia if the concentration of Hb falls below 7 g/dl (70 g/l). Even a less significant fall in the Hb concentration may cause symptoms in patients with heart or lung diseases.
- An Hb concentration of about 9–10 g/dl (90–100 g/l) is usually needed to safeguard adequate oxygen delivery.
- One unit of red cells typically raises Hb concentration by approximately 1 g/dl (10 g/l).

Acute or Massive Haemorrhage

- The replacement of blood loss in traumatic, surgical, obstetric or other haemorrhage necessitates, in addition to red cell transfusion, the substitution of platelets and coagulation factors. Refer to local guidelines that apply to the replacement procedures in major haemorrhage.

Selecting Red Cells for Transfusion

- Red cells are selected after compatibility testing (cross matching; see Picture 1 in the original guideline document) to ensure that the red cell units transfused are compatible with the recipient's ABO and RhD groups.
- RhD negative recipients are usually given RhD negative blood.
    - Transfusing RhD positive red cells is likely to trigger the production of anti-D antibodies, which is particularly harmful for girls and women with childbearing potential.
    - In extreme situations it may, however, be necessary to ignore this rule.
- O RhD negative red cells can be used for emergency transfusion before the patient's own blood group has been determined.
- Patients who have clinically significant red cell antibodies are given red cells that are phenotype matched.
    - In addition to matching the ABO and RhD blood-group systems, these red cells have undergone more extensive matching covering other blood-group antigens.
    - Ignoring clinically significant antibodies and transfusing blood without considering the blood-group antigens may result in haemolysis or other adverse transfusion reactions.
- Washed red cells are used in patients with a confirmed deficiency of immunoglobulin A (serum IgA <0.05 mg/l). Standard red cell products that contain plasma and IgA should not be administered to these patients. Moreover, washed red cells can be used in patients who experience recurrent severe allergic-type adverse reactions (e.g., fever, generalised urticaria and/or dyspnoea) associated with red cell transfusions.
    - A standard red cell product contains some residual plasma. Washing is carried out to remove some of the plasma and with it plasma proteins, which will result in symptom reduction.
- Irradiated red cells are used to prevent graft-versus-host reactions in immunosuppressed patients. Even though the blood products are filtered to remove white cells (leucodepleted) and the residual white cell count is very low, it is possible that small lymphocytes in particular pass the filter. Irradiation prevents lymphocyte proliferation and therefore prevents the development of a transfusion-associated graft-versus-host reaction.
    - Graft-versus-host reactions may develop when the lymphocytes in the transfused blood become activated in the new host.
    - Graft-versus-host reactions may occur in
        - Immunocompromised patients
        - Stem cell transplant recipients
        - Patients with haematological diseases
        - Foetuses receiving intrauterine transfusions
        - Small premature infants (<1500 g), very premature infants (<30 weeks of pregnancy)

Adverse Reactions Associated with Red Cell Transfusion

- Some adverse reactions typical to red cell transfusions are presented below, but during a transfusion the patient must be observed for any abnormal symptoms and, if indicated, local transfusion safety officials should be consulted about the possible connection between the symptoms and the transfusion.
- Febrile reaction
    - The most common reaction associated with red cell transfusions
    - Fever is a feature of almost all transfusion reactions. The treatment of a mild febrile reaction, with or without rigors, is symptomatic and no follow-up investigations are required.
    - The patient must be observed for the emergence of other symptoms which could signify a serious adverse reaction (e.g., sepsis or haemolytic reaction).
- Localised urticaria
    - A common transfusion reaction, the cause of which remains unknown. The patient is likely to be allergic to a component of the blood

product. Antihistamines will relieve symptoms. No follow-up investigations are required.

- Acute haemolysis
  - May lead to serious complications
  - The red cells are destroyed by the recipient's red cell antibodies; usually caused by a transfusion error (ABO incompatibility or other incorrectly matched transfusion).
  - Symptoms include fever, restlessness, chest and lower back pain, hypotension, respiratory distress, oliguria and anuria as well as disseminated intravascular coagulation (DIC)-induced bleeding. The urine will become brownish-red in colour.
  - The severity of symptoms is dependent on the number of red cells transfused and the patient's antibody levels.
  - Treatment concentrates on adequate hydration so as to prevent circulatory collapse and renal failure.
- Delayed haemolysis
  - Usually due to red cell antibodies which have been boosted by a secondary immune response.
  - The symptoms are usually milder than in acute haemolysis, and it is therefore likely that the condition is under-diagnosed.
  - Occurs about 1–4 weeks after a transfusion and the patient presents with jaundice, anaemia or an altered colour of the urine.
- Allergic reactions
  - Mild allergic reaction
    - Symptoms include urticaria, other pruritic erythema, localised angioedema or swelling of the lips, tongue or pharynx and eyelid oedema.
    - The reaction can be suspected to be caused by the transfusion if symptoms emerge during the transfusion or within 4 hours after its completion and no other cause, such as concurrent new medication, can be identified.
    - A common transfusion reaction, the cause of which remains unknown. The patient is likely to be allergic to a component of the blood product.
    - Antihistamines will relieve symptoms. No follow-up investigations are required.
  - Severe allergic reaction or anaphylaxis
    - Symptoms (dyspnoea, generalised urticaria, hypotension, nausea and loss of consciousness) may progress quickly to a serious, life-threatening situation.
    - Typically develops at the start of the transfusion but is also possible immediately after the transfusion has been completed
    - Anaphylaxis is rare.
    - Aetiology may involve the formation of anti-IgA antibodies against the transfused IgA in an IgA-deficient recipient. Plasma also contains soluble components and other proteins which could lead to symptoms in an allergic person.
    - Treatment is symptomatic, and careful planning is needed should the patient require transfusions in the future. It may be possible to prevent the reaction by using washed blood components (red cells and platelets). The aim of washing a blood product is to remove any residual plasma.
    - Standard red cell products that contain plasma and IgA cannot be transfused to a recipient with anti-IgA antibodies (contact local transfusion safety officials, if indicated)

Platelet Transfusion

- Platelet transfusions are used to control, or prevent, bleeding associated with medical procedures in patients with thrombocytopenia or platelet dysfunction.
  - One hour after a transfusion of 8 units of platelets (i.e., 2 packs = normal adult dose) the platelet count should increase by 40–50 × 10^9/l, and the morning after about 60% of the increase should still be present.
    - Poor response to platelet transfusions may be due to, for example:
      - Fever, sepsis, DIC, splenomegaly, certain drugs (amphotericin B, ciprofloxacin, vancomycin, heparin), vasculitis, graft-versus-host reaction
      - Immunological causes, such as human leukocyte antigen (HLA)-immunisation (common) or human platelet alloantigens (HPA)-immunisation (rare)
- Platelet transfusion in acute or massive haemorrhage
  - The replacement of blood loss in traumatic, surgical, obstetric or other haemorrhage necessitates, in addition to red cell transfusion, the substitution of platelets and coagulation factors. Refer to local guidelines that apply to the replacement procedures in major haemorrhage.

Selecting Platelets for Transfusion

- Platelets to be transfused are usually ABO- and RhD-compatible with the recipient.
- It is possible to transfuse ABO-incompatible platelets to manage an acute bleed or other transient deficiency state.

    - Transfusion response may slightly worsen.
- RhD negative recipients are usually given RhD negative blood.
    - Since a platelet concentrate will also contain some red cells, the RhD group must be considered when transfusing platelets. Transfusing RhD positive red cells is likely to trigger the production of anti-D antibodies, which is particularly harmful for girls and women with childbearing potential.
    - In extreme situations, or if RhD negative platelets are not available, it may be necessary to ignore this rule. The patient can be protected against RhD immunisation by administering human anti-D immunoglobulin (see the product's Summary of Product Characteristics for dosage instructions).
- There are two ways to obtain platelets for transfusion.
    - The standard platelet product is derived from the so-called puffy coat, and the platelets for one pack are pooled from 4 donors. Only a very small amount of plasma is present in this product. Some red cells are also present.
    - Apheresis platelets are prepared by collecting a larger amount from a single donor. For the present, this product contains plasma and therefore also the donor's anti-A and anti-B-isoagglutinins. An attempt is made to select platelets that match with the recipient's ABO and RhD groups. The collection of apheresis platelets is usually carried out for a specific need, for example for a transfusion of HLA-matched platelets.
- Irradiated products are used to prevent graft-versus-host reactions in immunosuppressed patients (see section Red Cell Transfusion above).

Adverse Reactions Associated with Platelet Transfusion

- Some adverse reactions typical to platelet transfusions are presented below, but during a transfusion the patient must be observed for any abnormal symptoms and, if indicated, local transfusion safety officials can be consulted about the possible connection between the symptoms and the transfusion.
- Febrile reaction
    - The most common reaction associated with platelet transfusions, which can be suspected to be caused by the transfusion if the fever starts during the transfusion, or within 4 hours after its completion, and no other cause can be identified.
    - Symptoms include either a rise in temperature to above 38°C or a rise of over 1°C from the pre-transfusion temperature. In some patients, the temperature does not rise but the patient has violent chills.
    - Fever is a feature of almost all transfusion reactions. The treatment of a mild febrile reaction, with or without rigors, is symptomatic and no follow-up investigations are required.
    - The patient must be observed for the emergence of other symptoms which could signify a serious adverse reaction (e.g., sepsis or haemolytic reaction).
- Allergic reactions: see section Red Cell Transfusion above.
- TRALI (transfusion associated acute lung injury)
    - TRALI is suspected in one out of 5000 transfusions.
    - Severe acute respiratory insufficiency is suggestive of TRALI.
    - TRALI is a clinical diagnosis, and typically there are no signs of concurrent volume overload or left ventricular failure, neither is there any evidence for the presence of other factors able to lead to acute respiratory insufficiency during or within 6 hours after completion of transfusion.
    - A chest x-ray will reveal bilateral pulmonary infiltrates.
    - Without prompt management TRALI may prove to be fatal.
    - The pathogenetic mechanism of TRALI is currently not fully understood. A possible cause proposed involves donor leucocyte antibodies (including anti-HLA and anti-HNA antibodies) which are introduced to the recipient in the residual plasma present in the transfused blood component. According to the theory the risk increases when more than 50 ml of plasma has been transfused, and TRALI is therefore rarely suspected with red cell transfusions. According to another hypothesis neutrophil-activating substances in the plasma (such as antibodies, cytokines) activate either the recipient's or the blood product's neutrophils. This would cause the neutrophils to attach to the lung endothelium, which in turn would lead to lung injury.
- Infections/sepsis
    - A septic reaction is caused by a transfusion of a blood product contaminated by bacteria.
    - Symptoms, which include high temperature and shock, usually emerge already during the transfusion or immediately after its completion.
    - The causative agent is a bacteria that originates from the donor's skin. Platelet products are more susceptible to contamination since their storage temperature is optimal to bacterial growth.
    - Other infections are very rare.
- PTP (post-transfusion purpura)
    - PTP is very rare.

- It is caused by a transfusion-triggered production of platelet-specific antibodies by the recipient. About a week after transfusion, the condition leads to thrombocytopenia with bleeding.
- If left untreated, serious complications are possible.
- Treatment consists of intravenous gammaglobulin.

Plasma Transfusion

- Plasma components used in most countries are so called fresh frozen plasma (FFP) components. Generally, they are frozen within 6–18 hours after the blood donation to preserve satisfactory levels of labile coagulation factors.
  - The component characteristics vary between the sites and local processing techniques.
  - FFP is thawed before administration, which may take up to 30–40 min depending on the amount of plasma thawed and techniques used.
  - Administration of FFP must be based on ABO-blood group compatibility. Depending on local instructions, RhD compatibility may be regarded as well.
  - The frozen plasma product Octaplas® is used in some countries. It is a registered medicinal product. See the Summary of Product Characteristics as regards its therapeutic indications, dosage and adverse effects.
  - In emergency cases, blood group AB (RhD negative) FFP (including blood group AB Octaplas®) can be regarded as universal plasma and it can be given to all patients.

Guidelines to the Treating Doctor Regarding Blood Transfusion

1. A medical practitioner must prescribe a blood transfusion.
   - The prescription must state the type of blood component (red cells, platelets, plasma), the volume to be transfused and any special requirements (irradiation, washing, phenotyping).
   - If necessary, instructions must be given regarding the speed of transfusion, the possible need to warm the product or any other factors to be considered due to, for example, the patient's condition, unless the staff have been issued relevant protocols.
   - If the patient has significant cold agglutinins, red blood cell products should be warmed during transfusion using an approved commercial blood warmer.
2. The person carrying out the transfusion must check the prescription and ensure that the red cell packs intended for transfusion have been found by the laboratory compatibility testing to be compatible with the recipient.
   - Before a transfusion of red cells, check the result of the compatibility testing and verify that the correct product and patient was used for the test: the donation number on the blood bag label must exactly match the number on the accompanying documentation and they must indicate the compatibility of the unit.
   - If the patient has red cell antibodies, ensure that the label on the red cell pack states the absence of the antigens corresponding to the antibodies detected in the patient (the label will state, for example, Jka - indicating the absence of antigen Jka).
3. The blood product must be checked for defects (integrity and cleanliness of the bag; the presence of clots, aggregates, gas or a black-red colour of a red blood cell product is suggestive of bacterial contamination; when inspecting platelet concentrates against light the presence of swirling should be observed).
4. Confirmation that the checks have been carried out is done by signing the transfusion form.
5. A blood administration set with an integral 150–200 µm filter, appropriately attached to the pack to be transfused, should be used to transfuse all blood products.
6. Verification of the patient's identity: the patient's identity data must be checked against the data on the blood product.
   - The patient is asked to state his/her identification (ID) details or
   - A person familiar with the patient verifies the identity of the patient (at the bedside); the identification details must also match with the patient's wristband
7. Before starting a transfusion, the patient's vital signs (heart rate, blood pressure, temperature) are checked and recorded. The start time of the transfusion must be recorded. The sticker on the blood product label indicating the unit number should be detached and reattached to the patient notes, or the transfusion is entered in the electronic patient record system.
   - The recording is carried out to fulfill the statutory obligation to ensure the traceability of the blood product from the recipient to the donor and vice versa.
8. If possible, a transfusion is started slowly with a biological pre-check.
   - During the first 10 minutes red cells are infused slowly (10–15 drops/min) whilst carefully observing the patient.
9. The same administration set may be used to transfuse several packs of red cells without interruption (according to the capacity of the administration set filter), but it is recommended that the administration set is changed after six hours in order to reduce the risk of bacterial contamination.

    - It is recommended that platelets are administered via a separate administration set or they may be transfused first, if transfusion is to continue with red cells. If the tubing has red cells, retention of platelets may occur.
10. Even though transfusion adverse effects often emerge at the beginning of transfusion, the patient must be monitored throughout the entire transfusion.
11. Red cell transfusion should be completed within six hours of removing the pack from the refrigerator to room air. The end time of the transfusion must be recorded.
12. The blood component pack with the administration set is recommended to be stored after transfusion for 24 hours in case adverse reaction investigations need to be carried out.

Suspicion of a Transfusion Reaction and/or Transfusion of a Wrong Blood Product

- Stop the transfusion immediately.
    - If a blood product destined for another patient has been transfused, the transfusion of wrong blood to the other patient must be prevented.
- The treatment of reactions follows the guidelines or general symptomatic treatment.
- Serious transfusion reactions must be reported to the appropriate local authorities.
    - A serious adverse reaction is defined as an untoward reaction associated with a blood transfusion in the recipient that might lead to death or is life threatening, or may lead to disability or incapacity, or which results in, or prolongs, hospitalisation or morbidity.
    - Country specific legislation will provide instructions regarding
        - The obligation of local health care units, blood banks, etc., to keep records relating to transfusion adverse effects and near miss incidents
        - The obligation to report serious adverse reactions, and near miss incidents, associated with blood quality and safety to the appropriate bodies
        - Recommendations to report other events, and near miss incidents, in order to promote the development of transfusion services.

Related Resources

Refer to the original guideline document for related evidence, including Cochrane reviews and other evidence summaries.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Chronic or slowly developing anaemia
- Acute or massive haemorrhage

Guideline Category

Management

Prevention

Clinical Specialty

Family Practice

Hematology

Internal Medicine

Nursing

Intended Users

Clinical Laboratory Personnel

Health Care Providers

Nurses

Physicians

Guideline Objective(s)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

Target Population

Patients in primary care settings who have anaemia (chronic or slowly developing) or haemorrhage (acute or massive)

Interventions and Practices Considered

1. Determining need for red blood cell (RBC) transfusion based on haemoglobin concentration and symptoms
2. Treatment of acute bleeding
    - Compatibility testing to ensure red cell units transfused are compatible with the recipient's ABO and RhD groups
    - Washed red cell products, including platelets
    - Irradiated red cells
3. Procedures for transfusion of blood products: RBCs, platelets, fresh frozen plasma
    - Laboratory compatibility testing
    - Checking procedures prior to transfusion (verifying patient identification, ensuring suitability of the product for the patient, ensuring integrity of the product)
    - Patient's vital signs
    - Administration of blood transfusion (started slowly but completed in six hours)

Major Outcomes Considered

Transfusion reactions

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The evidence reviewed was collected from the Cochrane Database of Systematic Reviews. In addition, the Cochrane Library and medical journals were searched specifically for original publications.

Comprehensive and systematic searches were conducted for all topics for which the Finnish Medical Society Duodecim produce national guidelines. As most of the evidence summaries were based on systematic reviews (of which Cochrane reviews were the most important), the search dates are available in the original reviews.

Specific Search Strategy

The update of this guideline includes several systematic reviews (with reported search dates) that are summarised in the "Related Resources" of the original guideline document. No search dates were given for the entire guideline.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Classification of the Quality of Evidence

Code	Quality of Evidence	Definition
A	High	Further research is very unlikely to change confidence in the estimate of effect. • Several high-quality studies with consistent results • In special cases: one large, high-quality multi-centre trial
B	Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate. • One high-quality study • Several studies with some limitations
C	Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. • One or more studies with severe limitations
D	Very Low	Any estimate of effect is very uncertain. • Expert opinion • No direct research evidence • One or more studies with very severe limitations

GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group 2011 (modified by the EBM Guidelines Editorial Team).

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

Not stated

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate administration of transfusions to patients with anaemia (chronic or slowly developing) or haemorrhage (acute or massive)

Potential Harms

- Bacterial contamination of blood or blood products
- Transfusion reactions
- Graft-versus-host reaction

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Safety

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2000 Mar 30 (revised 2011 Aug 15)

Guideline Developer(s)

Finnish Medical Society Duodecim - Professional Association

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Finnish Medical Society Duodecim

Guideline Committee

Editorial Team of EBM Guidelines

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

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This guideline updates a previous version: Finnish Medical Society Duodecim. Blood transfusion: indications and administration. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2008 Jan 10 [Various].

Guideline Availability

This guideline is included in "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

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